JACC: CARDIOVASCULAR IMAGING
VOL. 4, NO. 11, 2011

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2011.09.006

iCONCEPTS

CONCEPTS ON THE VERGE OF TRANSLATION

Intracoronary Transluminal Attenuation Gradient in Coronary CT Angiography for Determining Coronary Artery Stenosis

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Coronary computed tomography angiography (CTA) assessment of calcified or complex coronary lesions is frequently challenging. Transluminal attenuation gradient (TAG), defined as the linear regression coefficient between luminal attenuation and axial distance, has a potential to evaluate the degree of coronary stenosis. We examined the value of TAG in determining the stenosis severity on 64-slice coronary CTA. The value of TAG of 370 major coronary arteries was measured from 7,263 intervals of 5-mm length. Compared with coronary CTA and invasive coronary angiography, TAG decreased consistently and significantly with maximum stenosis severity on a per-vessel basis, from -1.91 ± 4.25 Hounsfield units/10 mm for diameter stenosis of 0% to 49% to -13.37 ± 9.81 Hounsfield units/10 mm for diameter stenosis of 100% ($p < 0.0001$). Adding TAG to the interpretation of coronary CTA improved diagnostic accuracy ($p = 0.001$), especially in vessels with calcified lesions ($N = 127$; net reclassification improvement 0.095; $p = 0.046$). TAG appears to be able to contribute to improved classification of coronary artery stenosis severity in coronary CTA, especially in severely calcified lesions. (J Am Coll Cardiol Img 2011;4:1149–57) © 2011 by the American College of Cardiology Foundation

Despite vast technological advancement, accurate classification of coronary stenosis severity by coronary computed tomography angiography (CTA) can be challenging because of the limited spatial resolution and frequent imaging artifacts related to calcification or motion that preclude confident assessment of the coronary artery lumen.

Transluminal attenuation gradient (TAG), defined as the gradient of intraluminal radiological attenuation, is a novel process that can evaluate the severity of coronary artery stenosis. TAG correlated linearly with the degree of coronary artery diameter stenosis in ex vivo studies and could discern normal and obstruc-

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tive coronary arteries in in vivo animal and human studies (1,2). We hypothesized that determination of TAG adds value in determining the severity of coronary complex or calcified coronary artery lesions. We measured TAG of major epicardial coronary arteries in patients with high-grade coronary artery disease (CAD) and compared it with the stenosis severity determined by invasive coronary angiography (CAG) as well as coronary CTA.

See page 1158

Methods

Patients. We retrospectively evaluated coronary CTA from 126 consecutive patients with at least 1 totally occlusive coronary artery lesion or multivessel CAD and who had undergone diagnostic CAG within 8 weeks between January 2007 and April 2009 at the Samsung Medical Center, Seoul, Korea. Patients with more than 50% stenosis in the left main coronary artery, acute coronary syndrome within 90 days, or intractable heart failure were not included. The institutional review board committee approved the study protocol.

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CAG = coronary angiography

CTA = computed tomography angiography

cTFC = corrected TIMI frame count

DS = diameter stenosis

HU = Hounsfield unit

NRI = net reclassification improvement

TAG = transluminal attenuation gradient

TIMI = thrombolysis in myocardial infarction

Quantitative analysis of invasive coronary angiography. The diameter stenosis (DS) of each major epicardial coronary artery was evaluated using quantitative coronary angiography (QCA) (Medis QAngio XA 7.1, Leiden, the Netherlands). The flow in each epicardial coronary artery was assessed with the use of the Thrombolysis In Myocardial Infarction (TIMI) grade as well as the TIMI frame count (TFC). In case of total occlusions, the degree of collateral flow was determined by Rentrop grade.

Coronary CTA image acquisition and reconstruction. Coronary CTA was performed with a 64-slice multidetector-row scanner (Aquilion 64, Toshiba Medical Systems, Tokyo, Japan). The scanning parameters were set to 120 kV, 400 mAs, 64 × 0.5 mm collimation, 0.4-mm increment, and 0.4-s tube rotation time. Estimated radiation dose ranged between 6 and 18 mSv.

A biphasic intravenous contrast injection protocol was used that consisted of 65 ml of nonionic contrast medium (iomeprol, 350 mg/ml, Bracco, Milan, Italy) at a flow rate of 4 ml/s followed by 30 ml of mixed normal saline (70%) and contrast medium (30%) at a rate of 3 ml/s. The image was reconstructed with use of retrospective electrocardiographic gating. Reconstructed slice thickness was 0.625 mm with a slice overlap of 33%.

Coronary artery analysis in coronary CTA. A dedicated workstation (GE advantage workstation 4.3, GE Healthcare, Milwaukee, Wisconsin) was used for analysis. The coronary artery tree was divided into 16 segments, and each segment was analyzed for the composition of plaque and degree of luminal stenosis. Plaque composition was classified as noncalcified (<30% calcified plaque volume), partially calcified (30% to 70%), or calcified plaque (>70%) according to the volume of calcific component (>130 Hounsfield units [HU]) in the plaque. The severity of luminal stenosis was classified and expressed on an ordinal scale as 0 (none; DS 0%), 1 (very mild; 1% to 29%), 2 (mild; 30% to 49%), 3 (moderate; 50% to 69%), 4 (severe; 70% to 99%), or 5 (total occlusion; 100%). For the analysis of maximum stenosis in each vessel, no to mild stenoses were combined into a single category. Segment stenosis score (0 to 15), the sum of maximal stenosis grade (0 to 5) in each of the 3 major epicardial coronary arteries, and segments at risk score (0 to 15), in which proximal segments were weighted, were calculated in a manner that we have described previously (3) to reflect the overall burden of obstructive CAD and the higher contribution to ischemia in proximal coronary segment, respectively.

Transluminal attenuation gradient. Cross-sectional images perpendicular to the vessel centerline were reconstructed for each major coronary artery. The following variables were measured at 5-mm intervals, from the ostium to the distal level where the vessel cross-sectional area fell below 2.0 mm^2: lumen cross-sectional area (mm^2), mean diameter (mm), and luminal radiological attenuation (HU). The contour of the region of interest and the vessel

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Manuscript received June 14, 2011; revised manuscript received August 8, 2011, accepted September 1, 2011.

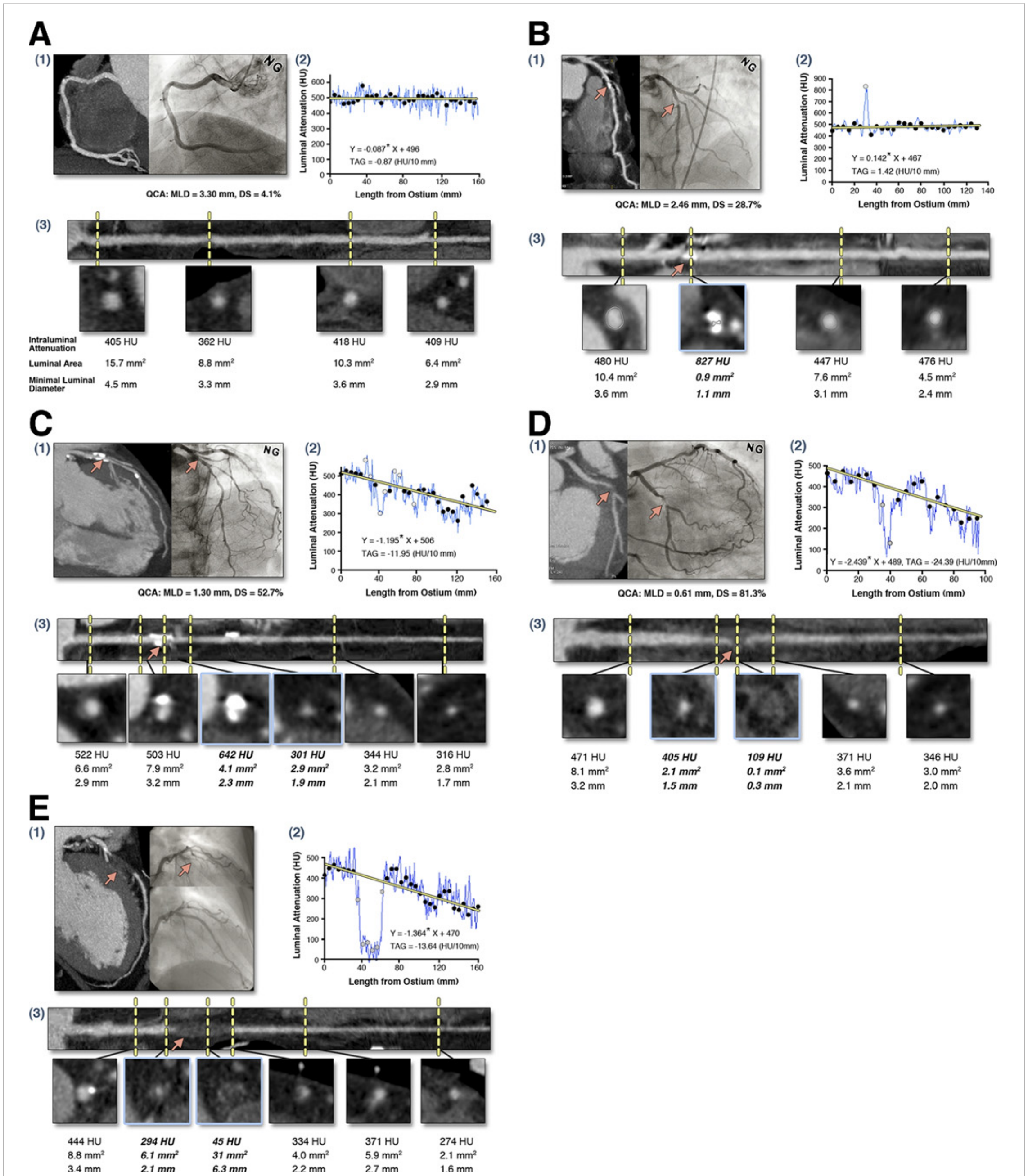

Figure 1. Representative Examples of Transluminal Attenuation Gradient Measurements

(A1) Right coronary artery with minimal obstructive plaque burden imaged by coronary computed tomography angiography (coronary CTA) and coronary angiography (CAG). **(A2) Black dots** represent 5-mm intervals at which intraluminal attenuation (Hounsfield units [HU]) and luminal area (mm^2) were measured. Transluminal attenuation gradient (TAG) is shown **(yellow line)** (−0.87 HU/10 mm). **(A3)** Axial and representative cross-sectional views of coronary CTA. **(B1)** Calcified lesion in mid–left anterior descending (LAD) artery that was indeterminate by coronary CTA, but diameter stenosis (DS) was 28.7% by quantitative coronary angiography. **Red arrows** indicate the most stenotic sites. **(B2) Grey dots** represent intervals that were excluded because of significant calcification or significant (DS >50%) stenosis. **(B3)** Cross sectional views with **grey border and sloped legend in italics** represent excluded intervals. The intraluminal attenuation in distal LAD artery does not decrease, demonstrating no significant obstruction. **(C1)** Coronary CTA demonstrates calcified lesions in proximal LAD artery and moderate stenosis in mid-LAD artery, confirmed by CAG. **(C2)** The linear correlation coefficient of **black dots**, TAG, is negatively sloped (−11.95 (HU/10mm). **(C3)** Decrease of intraluminal attenuation in distal vessel is shown. **(D)** Severe stenosis is shown in both coronary CTA and CAG. It is confirmed in cross-sectional views. **(E1)** Total occlusion is shown in both coronary CTA and CAG. **(E2)** TAG is severely negative (−13.64 HU/10mm). **(E3)** The cross-sectional views show exclusion of the intervals in the actual lesion from the calculation of TAG. MLD = minimal luminal diameter.

centerline were manually corrected if necessary. TAG was determined from the change in HU per 10-mm length of coronary artery and defined as the linear regression coefficient between intraluminal radiological attenuation (HU) and length from the ostium (mm). Representative examples are shown in Figure 1.

The stenosis and plaque characteristics were evaluated in each lesion. Vessels were classified as having noncalcified lesions if the most stenotic portion was noncalcified and as having calcified lesions if the most stenotic portion was calcified or partially calcified. Segment stenosis scores, segments at risk scores, and the maximum stenosis were evaluated in each vessel and compared with the TAG on a per-vessel basis.

Statistical analysis. All analysis was done on a per-vessel basis, and no adjustments were made for multiple vessels or segments within individuals. Continuous and categorical variables were compared using *t* test, analysis of variance, Kruskal-Wallis test, or Fisher exact test, as appropriate. Relationships between 2 continuous variables and continuous and categorical variables were tested by the Pearson correlation coefficient and Jonckheere-Terpstra test for trend, respectively. Diagnostic performance was compared using a global chi-square test and receiver-operator characteristic analysis with the DeLong method. Optimal cutoffs were determined by values with Youden *J* statistics.

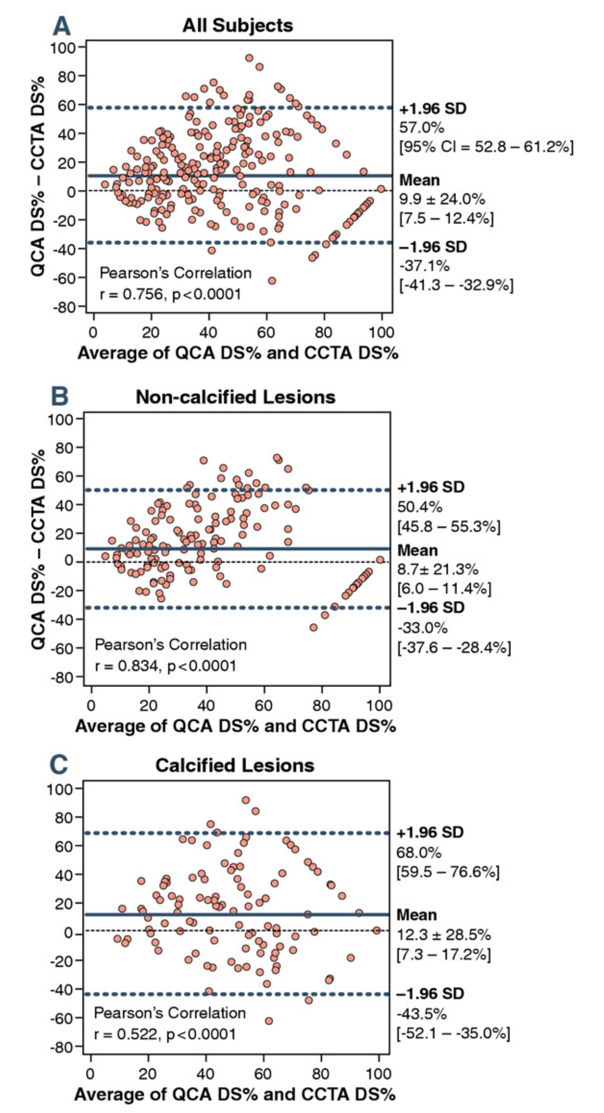

Figure 2. DS by Coronary CTA and CAG

DS by coronary CTA and DS by CAG were not different between vessels with calcified lesions and noncalcified lesions (mean difference 12.3 ± 28.5% vs. 8.7 ± 21.3%, Bland-Altman plot; p = 0.12, *t* test). The correlation between DS by coronary CTA and DS by CAG was significantly lower in vessels with calcified lesions than vessels with noncalcified lesions (Pearson correlation coefficient r = 0.522 vs. 0.834; p < 0.0001). Abbreviations as in Figure 1.

Table 1. Clinical Characteristics (N = 126)

Age, yrs	61.4 ± 10.8
Male	100 (78.7)
Body mass index, kg/m^2	25.3 ± 3.2
Hypertension	87 (69.0)
Diabetes	40 (31.7)
Hyperlipidemia	47 (37.3)
Smoking	34 (27.0)
Maintenance dialysis	3 (2.4)
Stroke	9 (7.1)
Hemoglobin, g/dl	14.13 ± 1.72
Creatinine, g/dl*	0.97 ± 0.19
C-reactive protein, mg/dl	0.44 ± 1.82
Electrocardiography	
Sinus rhythm	126 (100)
Left bundle branch block	0 (0)
Anterior Q wave	9 (7.1)
Inferior Q wave	7 (5.6)
Echocardiography†	
LV ejection fraction, %	58.1 ± 9.9
LV wall motion index	1.199 ± 0.330
Diagnosis	
Stable angina	75 (59.5)
Silent ischemia	18 (14.3)
Unstable angina	33 (26.2)
Coronary artery disease‡	
1-vessel disease	12 (9.5)
2-vessel disease	51 (40.5)
3-vessel disease	63 (50.0)

Values are mean ± SD or n (%). *Maintenance dialysis (n = 3) was excluded. †Echocardiography in 119 (94.4%). ‡Coronary artery disease was defined by coronary angiography.
LV = left ventricular.

The additional improvement of diagnostic performance after addition of TAG to the DS assessment in coronary CTA was evaluated using the net reclassification improvement index. The inter-rate agreement and reproducibility of TAG measurement was validated in 21 randomly selected vessels using Bland-Altman analysis and Cohen weighted kappa. SPSS version 13.0 (SPSS Inc., Chicago, Illinois) was used for most analyses except receiver-operating characteristic and Youden *J* statistics, which were accomplished using Medcalc version 11.4.1 (MedCalc Software, Mariakerke, Belgium). A 2-tailed p value <0.05 was considered statistically significant.

Results

Clinical characteristics. The clinical characteristics of the study population are summarized in Table 1. Of 378 coronary arteries, 8 hypoplastic vessels (6 left circumflex arteries, 2 right coronary arteries) were excluded. Significant stenosis (DS ≥50%) was present in 244 of 370 (65.9%) vessels (Table 2). Of 9,382 5-mm intervals obtained from 370 vessels, 2,119 intervals (22.7%) with ≥50% luminal DS (1,681 intervals), severe calcification (277 intervals), or stent (161 intervals) were excluded because of nonlinearity of luminal attenuation. Data from the remaining 7,263 intervals (77.3%) were used for the calculation of TAG.

TAG measures of reproducibility and agreement. For stenosis by coronary CTA, weighted kappa for intraobserver variability was 0.809 (95% confidence interval [CI]: 0.662 to 0.990) and for interobserver variability, 0.826 (95% CI: 0.668 to 0.950), respectively. For TAG, the limits of agreement by Bland-Altman analysis were 0.524 HU/10 mm (95% CI: −0.236 to 1.284) for repeated measurements by the same observer and −0.162 HU/10 mm (95% CI: −1.095 to 0.770) between different observers.

Impact of plaque composition on the accuracy of stenosis severity determined by coronary CTA. The degree and distribution of luminal stenoses in each coronary artery is shown in Table 2. The correlation between DS determined by coronary CTA and CAG was investigated. To facilitate analysis, partially calcified plaques (n = 16) and stented segments (n = 10) were included in the calcified plaque group, for a total of 127 cases. The agreement of DS was insignificant between calcified and noncalcified plaque lesions (mean difference 12.3 ± 28.5% vs. 8.7 ± 21.3% by Bland-Altman plot; p =

Table 2. Plaque Characteristics Classified by Luminal Stenosis Determined by Coronary CTA and ICA

		Diameter Stenosis by CAG QCA				
	All (N = 370)	0% to 49% (n = 126)	50% to 69% (n = 68)	70% to 99% (n = 55)	100% (n = 121)	p Value*
Vessel						
LAD	34.1 (126)	30.2 (38)	52.9 (36)	32.7 (18)	28.1 (34)	
LCx	32.4 (120)	39.7 (50)	33.8 (23)	40.0 (22)	20.7 (25)	0.0009
RCA	33.5 (124)	30.2 (38)	13.2 (9)	27.3 (15)	51.2 (62)	
CAG						
RD, mm	2.79 ± 0.60	3.08 ± 0.59	2.61 ± 0.54	2.55 ± 0.58	2.69 ± 0.55	<0.0001
MLD, mm	1.02 ± 1.00	2.20 ± 0.59	1.08 ± 0.31	0.51 ± 0.18	0.00 ± 0.00	<0.0001
TIMI grade	2.02 ± 1.25	2.93 ± 0.26	2.93 ± 0.32	2.11 ± 1.03	0.51 ± 0.74	<0.0001
Rentrop grade	0.50 ± 0.74	0.01 ± 0.09	0.03 ± 0.17	0.36 ± 0.62	1.34 ± 0.61	<0.0001
Coronary CTA						
RD, mm	3.26 ± 0.63	3.38 ± 0.63	3.26 ± 0.51	3.00 ± 0.69	3.25 ± 0.62	0.002
MLD, mm	1.48 ± 1.23	2.52 ± 0.70	1.76 ± 0.90	1.43 ± 1.09	0.25 ± 0.68	<0.0001
Ostial diameter, mm	4.26 ± 0.95	4.35 ± 0.99	4.29 ± 1.07	4.32 ± 0.85	4.14 ± 0.93	0.38
Most distal diameter, mm	1.94 ± 0.44	2.16 ± 0.44	2.00 ± 0.42	1.92 ± 0.48	1.78 ± 0.36	<0.0001
Plaque composition						
Noncalcified	65.7 (243)	66.7 (84)	41.2 (28)	70.9 (39)	76.0 (92)	
Calcified	27.3 (101)	24.6 (31)	50.0 (34)	21.8 (12)	19.8 (24)	<0.0001
Partially calcified	4.3 (16)	5.6 (7)	5.9 (4)	5.5 (3)	1.7 (2)	
Stented	2.7 (10)	3.2 (4)	2.9 (2)	1.8 (1)	2.5 (3)	
Vessel length, mm	122.1 ± 29.0	121.1 ± 30.6	122.2 ± 31.8	114.6 ± 25.6	126.6 ± 26.6	0.08

Values are n (%) or mean ± SD. Plaque composition analysis: vessels with noncalcified lesions were compared with the other vessels. *p Value by analysis of variance, Kruskal-Wallis test, or chi-square test.
CAG = coronary angiography; CTA = computed tomography angiography; ICA = invasive coronary angiography; LAD = left anterior descending; LCx = left circumflex; MLD = minimal luminal diameter; QCA = quantitative coronary angiography; RCA = right coronary artery; RD = reference diameter; TIMI = Thrombolysis In Myocardial Infarction.

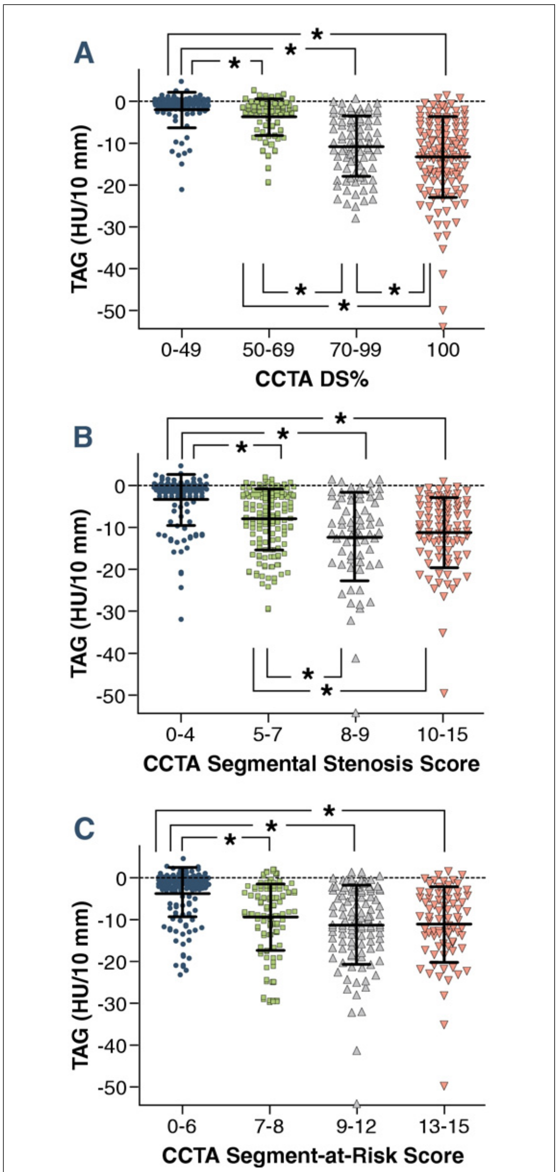

Figure 3. TAG in Relation to Luminal Stenosis Severity by Coronary CTA

(A) TAG versus DS by coronary CTA. DS 0% to 49%, n = 84, −1.91 ± 4.25 HU/10 mm; DS 50% to 69%, n = 68, −3.54 ± 4.43; DS 70% to 99%, n = 87, −10.55 ± 7.20; DS 100%, n = 131, −13.37 ± 9.81 ($p < 0.0001$ by analysis of variance [ANOVA], $p < 0.0001$ by Jonckheere-Terpstra test). *$p < 0.05$ by *t* test between 2 groups. **(B)** TAG versus segmental stenosis score. First quartile (score 0 to 4), n = 100, −3.37 ± 6.12 HU/10 mm; second quartile (5 to 7), n = 113, −7.90 ± 7.52; third quartile (8 to 9), n = 68, −12.22 ± 10.74; fourth quartile (10 to 15), n = 89, −11.35 ± 8.57 ($p < 0.0001$, respectively). **(C)** TAG versus segment at risk score. First quartile (score 0 to 6), n = 124, −3.50 ± 5.86 HU/10 mm; second quartile (7 to 8), n = 64, −9.33 ± 8.13; third quartile (9 to 12), n = 107, −11.18 ± 9.54; fourth quartile (13 to 15), n = 75, −11.23 ± 9.05 ($p < 0.0001$, respectively). Abbreviations as in Figure 1.

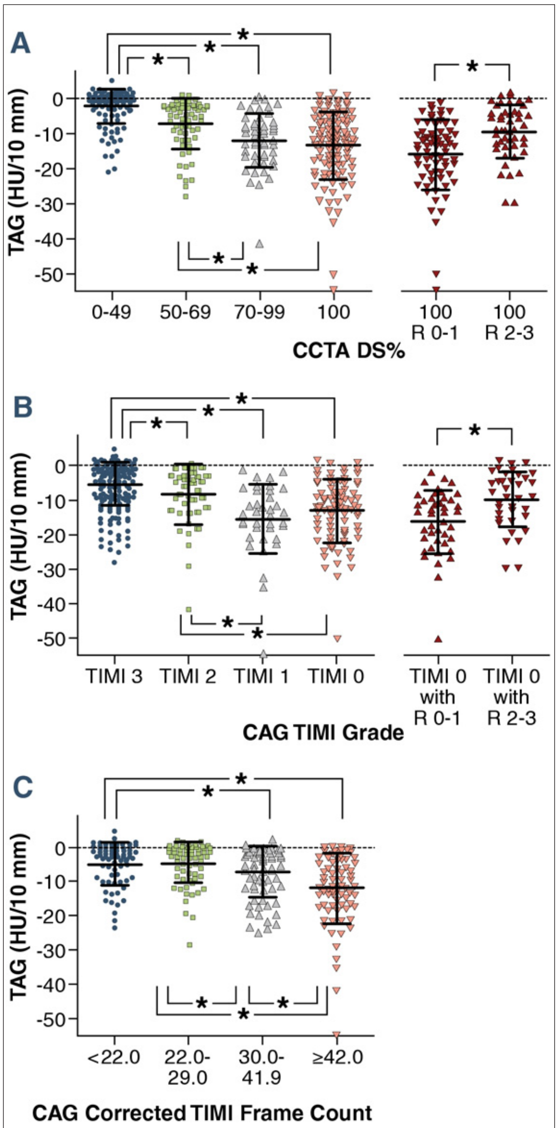

Figure 4. TAG in Relation to Luminal Stenosis Severity and Coronary Artery Flow Velocity by Invasive Coronary Angiography

(A) TAG versus DS by CAG. DS 0% to 49%, n = 126, −2.37 ± 4.67 HU/10 mm; DS 50% to 69%, n = 68, −7.18 ± 6.91; DS 70% to 99%, n = 55, −11.91 ± 7.61; DS 100%, n = 121, −13.46 ± 9.59 ($p < 0.0001$ by ANOVA, $p < 0.0001$ by Jonckheere-Terpstra test). TAG of DS 100% with Rentrop grade 0 to 1 was lower than moderate (DS 50% to 69%) or severe (70% to 99%) stenosis ($p < 0.001$ and $p = 0.011$, respectively). TAG of total occlusion with Rentrop grade 2 to 3 and moderate or severe stenosis were comparable ($p = 0.09$ and $p = 0.12$, respectively). **(B)** TAG versus Thrombolysis In Myocardial Infarction (TIMI) grade. TIMI 3, n = 208, −5.14 ± 6.57 HU/10 mm; TIMI 2, n = 42, −8.27 ± 8.86 HU/10 mm; TIMI 1, n = 38, −15.31 ± 10.14 HU/10 mm; TIMI 0, n = 82, −13.06 ± 9.15 HU/10 mm ($p < 0.0001$, respectively). TIMI 0 with Rentrop collateral grade 0 to 1, n = 44, −15.95 ± 9.11; TIMI 0 with Rentrop collateral grade 2 to 3, n = 38, −9.72 ± 8.09 ($p = 0.002$). **(C)** TAG versus corrected TIMI frame count (cTFC) quartiles (n = 288, TIMI 0 flow were excluded). First quartile (<22), n = 70, −4.63 ± 6.16 HU/10 mm; second quartile (22 to 29.9), n = 74, −4.27 ± 5.94; third quartile (30 to 41.9), n = 70, −6.95 ± 7.28; fourth quartile (≥42), n = 74, −11.79 ± 10.39 ($p<0.0001$, respectively).

0.12 by unpaired t test), but the correlation of stenosis severity was significantly lower for calcified lesions than for noncalcified lesions (Pearson correlation coefficient $r = 0.522$ vs. 0.834; $p < 0.0001$) (Fig. 2).

TAG in relation to luminal stenosis severity by coronary CTA. TAG decreased progressively according to the severity of stenosis as determined by coronary CTA: -1.91 ± 4.25 HU/10 mm for DS 0% to 49% (n = 84), -3.54 ± 4.43 HU/10 mm for DS 50% to 69%, -10.55 ± 7.20 HU/10 mm for DS 70% to 99%, and -13.37 ± 9.81 HU/10 mm for DS 100% ($p < 0.0001$) (Fig. 3A). TAG also decreased according to the quartiles of the segmental stenosis score and segment at risk score, which represent overall burden of obstructive disease and potential risk evoked by proximal lesion, respectively ($p < 0.0001$) (Figs. 3B and 3C).

TAG in relation to luminal stenosis severity by CAG. TAG decreased as stenosis severity determined by CAG increased, from -2.37 ± 4.67 HU/10 mm for DS 0% to 49% to -13.46 ± 9.59 HU/10 mm for DS 100% ($p < 0.0001$) (Fig. 4A). The relationship between TAG and stenosis severity determined by CAG was consistent in subgroup analysis examining different vessel territories or plaque compositions (Table 3). TAG was also related to the coronary flow velocity as determined by TIMI grade, corrected TIMI frame count (cTFC), and Rentrop scale of collateral flow (all $p < 0.0001$) (Figs. 4B and 4C). Among totally occluded arteries (TIMI grade 0), TAG was lower in vessels with Rentrop grade 0 to 1 collaterals (-16.04 ± 9.93 HU/10 mm) than with grade 2 to 3 collateral (-9.54 ± 7.62 HU/10 mm) ($p < 0.0001$). TAG of totally occluded vessels with Rentrop grade 0 to 1 collateral flow was significantly lower than TAG of moderate (50% to 69%) or severe (70% to 99%) stenoses ($p < 0.001$ and $p = 0.011$, respectively). TAG of totally occluded vessels with Rentrop grade 2 to 3 collateral flow was comparable to TAG of moderate or severe stenosis (p = nonsignificant) (Fig. 4B).

Effect of TAG on reclassification of coronary CTA stenosis severity. The accuracy of stenosis severity classification by coronary CTA, compared with CAG, improved significantly when TAG was taken into account (c statistic 0.932 ± 0.012 vs. $0.951 \pm$

Table 3. TAG Subgroup Analyses Examining Different Vessel Territories or Plaque Compositions

				p Value		
	CAG Stenosis	n	TAG (HU/10 mm)	vs. 50% to 69% Stenosis	vs. 70% to 99% Stenosis	vs. 100% Stenosis
All	0% to 49%	126	−2.37 ± 4.67	<0.001	<0.001	<0.001
	50% to 69%	68	−7.18 ± 6.91	—	<0.001	<0.001
	70% to 99%	55	−11.91 ± 7.61	—	—	0.29
	100%	121	−13.46 ± 9.59	—	—	—
LAD	0% to 49%	38	−2.93 ± 5.14	0.003	<0.0001	<0.0001
	50% to 69%	36	−7.05 ± 6.45	—	0.015	<0.0001
	70% to 99%	18	−11.60 ± 5.91	—	—	0.09
	100%	34	−16.05 ± 9.82	—	—	—
LCx	0% to 49%	50	−3.62 ± 5.16	0.001	<0.0001	<0.0001
	50% to 69%	23	−8.94 ± 7.89	—	0.05	<0.0001
	70% to 99%	22	−13.99 ± 9.18	—	—	0.015
	100%	25	−21.19 ± 10.16	—	—	—
RCA	0% to 49%	38	−0.16 ± 2.08	0.004	<0.0001	<0.0001
	50% to 69%	9	−3.18 ± 4.45	—	0.019	0.01
	70% to 99%	15	−9.24 ± 6.30	—	—	0.86
	100%	62	−8.93 ± 6.26	—	—	—
Noncalcified lesion	0% to 49%	84	−2.69 ± 5.00	<0.0001	<0.0001	<0.0001
	50% to 69%	28	−6.92 ± 6.06	—	0.002	0.002
	70% to 99%	39	−12.80 ± 8.09	—	—	0.79
	100%	92	−13.28 ± 10.00	—	—	—
Calcified lesion	0% to 49%	42	−1.72 ± 3.89	<0.0001	<0.0001	<0.0001
	50% to 69%	40	−7.36 ± 7.51	—	0.263	0.001
	70% to 99%	16	−9.74 ± 5.95	—	—	0.08
	100%	29	−14.04 ± 8.45	—	—	—

HU = Hounsfield unit; TAG = transluminal attenuation gradient; other abbreviations as in Table 2.

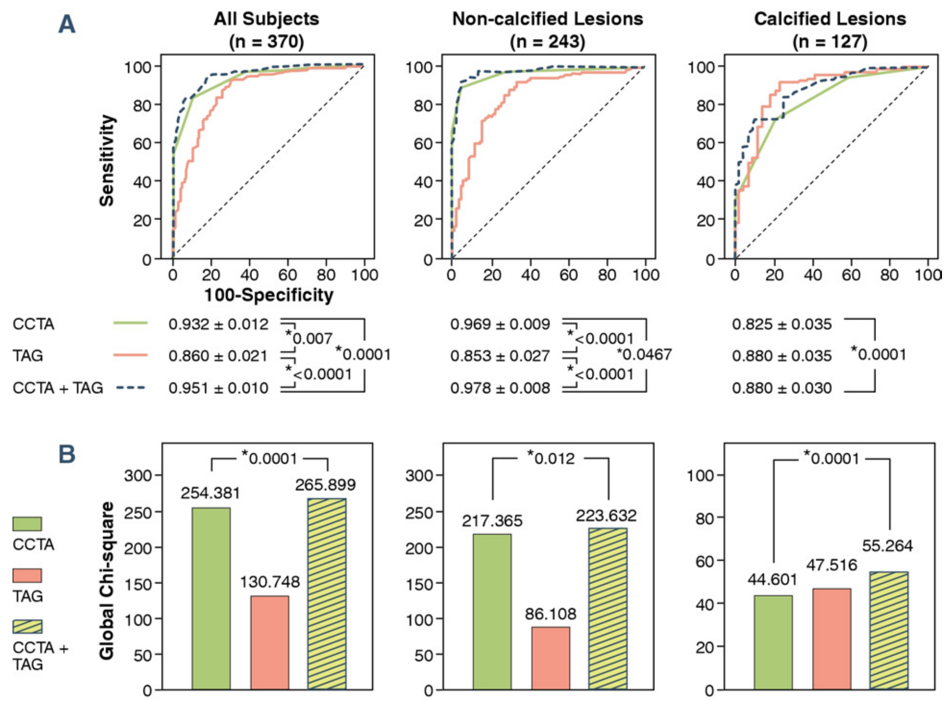

Figure 5. Effect of TAG on Reclassification of Coronary CTA Stenosis Severity

(A) *C*-statistics are compared pairwise using the DeLong method. Predicted probability from a logistic regression equation was used for addition of TAG (regression coefficient −1.119, p = 0.001) to coronary CTA (1.935, p < 0.001). **(B)** Global chi-squares are shown in each graph. *p < 0.05. Abbreviations as in Figure 1.

0.010, p = 0.001; global chi-square 254.381 vs. 265.899, p = 0.001). The improved diagnostic accuracy was mainly driven by increased specificity (89.7% [95% CI: 83.0 to 94.4] vs. 93.7% [95% CI: 87.9 to 97.2]). TAG also added value to the diagnostic accuracy of coronary CTA for types of plaque that make visual estimation difficult. The diagnostic accuracy of coronary CTA was significantly lower for vessels with calcified lesions than for vessels with noncalcified lesions (p < 0.0001). The accuracy of severity classification of calcified stenoses by coronary CTA significantly increased when TAG was taken into account (*c* statistic, p < 0.0001; global chi-square, p = 0.001). TAG also improved the accuracy of the severity classification of stenoses caused by noncalcified plaques (*c* statistic, p = 0.048; global chi-square, p = 0.012) (Fig. 5, Table 4).

The addition of TAG resulted in reclassification from one class of stenosis severity to another in a significant number of vessels with calcified lesions (net reclassification improvement [NRI] 0.095, net proportion of patients reclassified 3.15%; p = 0.046). Addition of TAG did not result in significant stenosis severity reclassification in vessels with noncalcified lesions (NRI −0.006; p = 0.56) or in the entire cohort (NRI 0.036; p = 0.06).

Our study showed that TAG, which provides information on the functional significance of coronary artery stenoses by reflecting the gradient of intralumi-

Table 4. Incremental Value of TAG to the Diagnostic Performance of Coronary CTA

Optimal Cutoff	*C*-Statistics	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
TAG: >−1.80 HU/10 mm	0.860 ± 0.021 (0.820–0.894)	92.6 (88.6–95.6)	69.1 (60.2–77.0)	85.3 (80.4–89.3)	82.9 (74.2–89.5)
Coronary CTA: DS ≥50%	0.932 ± 0.012 (0.902–0.956)	84.0 (78.8–88.4)	89.7 (83.0–94.4)	94.0 (90.0–96.8)	74.3 (66.6–81.1)
TAG + Coronary CTA: logistic regression probability >0.8056	0.951 ± 0.010 (0.924–0.971)	83.6 (78.4–88.0)	93.7 (87.9–97.2)	96.2 (92.7–98.4)	74.7 (67.1–81.3)

Values are mean ± SE (95% confidence interval) or % (95% confidence interval).
Abbreviations as in Tables 2 and 3.

nal attenuation across the lesion, can refine the classification of anatomic coronary CTA stenosis severity compared with CAG as a reference standard. TAG was related not only to the severity of stenosis but also to flow velocity. Although only limited in vessels with calcified lesions, TAG slightly but significantly improved the diagnostic accuracy of coronary CTA and could reclassify the diagnosis of coronary CTA.

Clinical Perspective

We validated TAG against angiographic binary stenosis. Comparison of this study to other functional studies including fractional flow reserve and myocardial perfusion imaging would be required to examine whether TAG can predict myocardial ischemia bases on coronary CTA studies. The following potential confounding parameters should be controlled when TAG is attempted. TAG depends on the luminal attenuation values, which are influenced by various artifacts including partial volume effects, image smoothing, plaque calcifications, and beam hardening. TAG also depends on the time-density curve of intravascular contrast agent and scanning time. A newly introduced 320-detector row scanner that enables single-beat imaging of the entire coronary tree may be ideal for TAG measurement.

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Key Words: computed tomography ■ coronary artery imaging ■ diagnosis of coronary artery stenosis.